

EXHIBIT E



Evaluation and Management of Mid-Urethral Sling Complications

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Abstract Currently, a mid-urethral sling is the standard of care for the treatment of female stress urinary incontinence. However, complications can occur that are unique to polypropylene mesh such as mesh exposure, perforation, or contracture. Other complications such as de novo urgency and/or urgency urinary incontinence (UUI), urinary tract infection, and/or urinary obstruction can also occur. The diagnosis of these complications requires a high index of suspicion, and treatment is critical as these complications can be quite morbid. As such, this review will discuss the most recent literature regarding the intraoperative and post-operative evaluation and management of mid-urethral sling complications.

Keywords Stress urinary incontinence · Mid-urethral sling · De novo urgency · Pelvic pain · Mesh perforation · Bladder outlet obstruction

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Introduction

Female stress urinary incontinence (SUI) is estimated to affect half of all adult women, though this number varies widely in the literature [1]. The true prevalence may actually be much higher as many women are hesitant to discuss incontinence with their healthcare providers [2]. This may be due to embarrassment or due to a preconceived notion that incontinence is a normal part of aging [3]. Definition differences for SUI throughout the literature may also contribute to the underestimation of SUI [4]. While the true prevalence of SUI is unknown, the cost of healthcare dollars devoted to urinary incontinence (UI) altogether is considerable. Estimates of indirect and direct costs of UI in the USA are approximately \$19.5 billion per year [5]. Despite the pervasiveness of SUI, surgical treatment options were historically limited to invasive therapies such as pubovaginal slings, suspension type procedures, or retropubic urethropexies until the development of the mid-urethral sling (MUS) [6].

Due to the short operative time, minimal morbidity, rapid convalescence, and long-term efficacy, the MUS is currently considered by many to be the standard of care for the treatment of SUI [7]. In 2010, approximately 260,000 American women underwent surgical correction for SUI, and over 80 % of these procedures were MUS [8]. The American Urological Association (AUA) Guideline for the surgical management of SUI supports this change in practice as estimated cured/dry rates in patients without concomitant prolapse treatment range from 81 to 84 %. This is comparable to results for the Burch suspensions and autologous fascial slings, showing comparable efficacy in the surgical treatment of SUI [9].

Currently, there are numerous MUS available for use. The traditional, multi-incision MUS can be surgically placed with either a retropubic (RP) or a transobturator (TOT) approach. These can be inserted top-down or bottom-up and outside-in

or inside-out, respectively [10]. There is also a newer generation of MUS—the “mini-sling”—only requiring a single vaginal incision and is meant to be located entirely within the pelvis, without any anterior abdominal wall or obturator support mechanism. Since there are so many variations of the MUS, compounding the complications of all MUS is challenging as each can have unique complications.

Nonetheless, certain complications from MUS surgery are unique to the use of polypropylene mesh. These can include mesh exposure, chronic pelvic pain, and dyspareunia, which are the most common, as well as mesh contracture, organ perforation, and/or neuromuscular injury. Other complications may include de novo urgency and/or urgency urinary incontinence (UUI), urinary tract infection (UTI), and/or urinary obstruction. As a result of these complications and the ensuing morbidity, it is imperative that when placing a mid-urethral sling, providers follow the AUA guidelines and have a high index of suspicion for intraoperative and post-operative complications [9•]. The evaluation and management of MUS complications are discussed herein.

Food and Drug Administration Notifications and the MUS

The plethora of MUS complications, in addition to those reported from transvaginal mesh (TVM) use in the treatment of pelvic organ prolapse (POP), led the Food and Drug Administration (FDA) to issue its first Public Health Notification in 2008 to inform patients of adverse events related to the use of mesh placed in the urogynecology setting. In 2011, the FDA released a Safety Communication, which reported complications with TVM for POP but did not include TVM for SUI.

Subsequently, in 2013, the FDA updated their recommendations regarding the use of TVM for SUI asserting that the currently marketed, multi-incision, mid-urethral polypropylene slings are safe and effective with a positive risk-to-benefit profile [11].

However, there is currently an overall paucity of data to truly estimate the complication profile of the mini-sling. As such, the FDA ordered post-market surveillance studies “522 studies” to be performed by manufacturers of urogynecologic surgical mesh to address specific safety and efficacy concerns related to mini-slings [11]. As of February 17, 2013, the FDA had issued 14 orders to 7 manufacturers of mesh used in mini-slings [12•, 13].

Similar to the FDA, the American Urogynecologic Society (AUGS) and the Society of Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction (SUFU) issued a joint position statement in 2014 strongly supporting the use of polypropylene mesh for the treatment of SUI, maintaining that the MUS procedure is safe, effective, and remains

the standard of care for the treatment of SUI [12••]. Additionally, the AUA position statement on the use of vaginal mesh for the surgical treatment of SUI states that the restriction of the use of synthetic multi-incision slings would be a disservice to women who choose surgical correction of SUI; however, single incision mini-slings are still currently undergoing further safety and efficacy trials [14•].

Nevertheless, there has been a plethora of litigation surrounding the placement of mesh for POP and SUI. Legal action has been taken against hospitals, surgeons, and mesh manufacturers [13]. Consequently, it is imperative that physicians provide clear, unambiguous informed consent that includes specific mesh-related risks when discussing any procedure involving mesh and document such in the medical record. The AUA, SUFU, and International Urogynecological Association (IUGA) have all issued detailed guidelines for consenting patients [14•, 15•]. Additionally, the FDA published their own guidelines for obtaining informed consent for mesh-related procedures. According to the FDA, providers should inform patients that (1) the implantation of surgical mesh is permanent and that some complications associated with mesh may require additional surgery that may or may not correct the complication and (2) there is potential for serious mesh-related complications that can have an effect on the quality of life, including dyspareunia, scarring, and vaginal wall narrowing [11]. The FDA strongly advises that providers explicitly state to patients that mesh will be used in surgery and recommends that written information about the specific mesh product be given to the patient.

Mid-Urethral Sling Complications

The overall rate of MUS complications is difficult to ascertain as there are limited randomized controlled trials (RCTs) with adequate follow-up—many complications can present much later than the defined study period. Furthermore, we do not currently have a mandatory reporting system for complications of MUS. In an effort to standardize terminology to facilitate the implementation of a reliable registry, the International Urogynecological Association (IUGA) and the International Continence Society (ICS) have endorsed a new classification system for complications related to prostheses in female pelvic floor surgery. In this report, synthetic mesh located within the bladder or urethra is termed a perforation and mesh extrusion through the vagina or skin is termed an exposure [16].

Nevertheless, there have been many retrospective and case-control studies reporting MUS complications. A recent case-control study by Unger et al. evaluated 3307 women who underwent MUS placement from 2003–2013 [17]. They reported an overall sling revision rate of 2.7 % for the following indications: urinary retention (43.8 %), voiding dysfunction (42.7 %), recurrent UTI (20.2 %), mesh erosion (21.3 %),

vaginal pain/dyspareunia (7.9 %), and groin pain (3.4 %). Furthermore, a tertiary care, multicenter, retrospective analysis also reported complications from MUS to be quite high. They identified 173 women who underwent a synthetic MUS without a concomitant prolapse repair and identified a mesh erosion/exposure/extrusion rate of 30.1 %, a urinary obstruction rate of 32.4 %, a voiding dysfunction rate of 34.7 %, a dyspareunia rate of 19.7 % and a recurrent or de novo incontinence rate of 35.5 % [18]. Approximately 50 % of the patients in this study underwent the MUS procedure at another institution. Another study by Katsuri et al. evaluated post-operative voiding dysfunction rates and retrospectively stratified them by the type of MUS. They estimated voiding dysfunction after MUS to be 2.8–38 % for a retropubic MUS and 0–15.6 % with the transobturator approach [19].

These complication rates appear much higher than those previously reported in RCTs such as the Trial of Mid-Urethral Slings (TOMUS). The TOMUS trial compared the efficacy and complication rates between retropubic and transobturator MUS in 597 women. The trial reported both subjective and objective equivalence between the two surgical approaches [20]. At 2-year follow-up, however, the study showed a higher rate of voiding dysfunction with RP sling placement compared to TOT: 3 versus 0 %, respectively ($p=0.002$) [21]. On the other hand, the TOT approach resulted in more neuromuscular complaints such as leg weakness, pain, and groin numbness when compared to RP MUS: 9.7 versus 5.4 %, respectively ($p=0.045$) [21]. The rates for de novo incontinence were 0 versus 0.3 % for RP and TOT, respectively ($p=0.99$). Overall, these complication rates shown in the TOMUS trial are much lower than those reported by the more recent retrospective studies, suggesting that complication data in a RCT can be limited. As such, we can extrapolate from the current studies that the overall complication rates are higher than originally reported and a lack of consistent follow-up with the initial surgeon may contribute to this.

Common Intraoperative Complications and Management

The best way prevent complications associated with a MUS procedure is to adhere to fundamental surgical practices during the insertion. These include appropriate knowledge of pelvic and vaginal anatomy; careful vaginal dissection and hemostasis; diligence during the passage of the sling trocars to avoid injury or perforation to the bladder, urethra, vaginal tissue, or groin structures; appropriate tensioning (i.e., “tension-free”) during sling deployment; and diligence for identifying intraoperative complications. In the case that a urethrotomy is made during the procedure, the MUS should not be placed. Intraoperative cystoscopy should also be performed at the time of sling placement according to the

standards in the AUA Guidelines on the surgical management of female SUI [9•]. Nevertheless, intraoperative complications can occur and must be managed accordingly.

Hemorrhage

Bleeding can occur with both the vaginal dissection and passage of the trocars. However, profuse bleeding during procedures for SUI is infrequent, with transfusion rates for all SUI procedures ranging from 1–4 % [9•]. If significant bleeding occurs during the vaginal dissection, it can indicate that the dissection is not in the correct surgical plane—a dissection immediately beneath the vaginal epithelium should not cause much bleeding. However, if the incision and/or dissection are too deep, the pubocervical fascia or urethral tissue can bleed copiously. Should this occur, redirect the dissection into the correct plane and gently control the bleeding with bipolar cautery.

Blind entry into the retropubic or transobturator space during dissection or trocar passage can also lead to bleeding. It is common for some venous bleeding to occur with the passage of the trocars. Most mild, venous bleeding can be controlled with passive tamponade by closing the vaginal epithelium expeditiously and inserting vaginal packing. However, obturator, iliac, and femoral vessel injuries have been reported [22]. In the retropubic approach, if the trocars are inserted too lateral, the pelvic vessels can be injured. For a transobturator approach, the trocars should be inserted into the inferior, medial aspect of the obturator foramen beneath the insertion of the adductor longus to prevent neurovascular injury.

If there is concern for significant bleeding, first ensure the availability of blood products and then maximize exposure and lighting. Vascular surgery may need to be consulted intraoperatively. Abdominal access to the retropubic space can be obtained through a lower midline incision. The pelvic hematoma may be significant and need to be compressed intermittently through anterior vaginal wall pressure. With localization of the bleeding, a 4-0 or 5-0 monofilament suture is used to repair the vessel. Hemostatic agents may also be used. If the bleeding is unable to be controlled, pack the pelvis and resuscitate the patient. The patient may then be brought back to the operating room at another time or arterial embolization by interventional radiology may be considered. Successful outcomes using embolization have also been reported for cases of profuse bleeding with the transobturator approach where direct visualization can be limited [22, 23].

Urinary Tract Injury

The lower urinary tract (LUT) is at risk for injury during any portion of the MUS procedure and, if unrecognized, can have significant ramifications. Specifically, passage of the MUS

trocars can cause injury to the bladder, urethra, or bladder neck. The urethra can also be injured during the vaginal dissection. Though rare, ureteral injury can also occur with passage of the MUS trocar near the trigone or with the vaginal dissection. Patients with an unrecognized LUT injury can develop mesh perforations in the bladder or urethra, vesico- or urethro-vaginal fistulae, bladder stones, gross hematuria, pelvic pain, and recurrent UTIs. As such, it is paramount that these injuries be identified intraoperatively. The rate of urinary tract injury with a trocar at the time of surgery ranges from 2.7–23.8 % [24].

To assess for LUT injury, intraoperative cystoscopy should always be performed with 70° and 30° lenses after trocar passage and with the trocars in place. The bladder should be fully filled to achieve complete expansion. The bladder as well as the bladder neck and urethra should be carefully inspected along the courses of the trocar. Urethroscopy can be difficult in women because of the short urethra, but diligence is required as urethral perforation can be subtle and poorly visualized. Ureteral patency should also be documented by identifying efflux of clear urine, and if there is concern for injury, a retrograde pyelogram should be performed—a JJ stent should be placed if extravasation occurs. If there is additional concern or suspicion, cystoscopy can be repeated after the deployment of the synthetic sling and trocar removal, as this can unmask previously unseen LUT perforations.

In an attempt to prevent LUT injuries, the MUS trocars should only be passed after the bladder is fully drained. A rigid urethral guide can be used to gently deflect the urethra to the contralateral side while the ipsilateral trocar is passed through the paraurethral space. However, if a bladder injury is identified during placement of a trocar, the offending trocar should be removed and re-passed. If there is concern for a large bladder defect, a Foley catheter may be left in place, but a small trocar puncture site typically closes without difficulty and prolonged catheterization is unnecessary. If a urethral injury occurs either during the vaginal dissection or with passage of the MUS trocar, mesh sling placement should be aborted. The urethral defect should be closed primarily and an indwelling Foley catheter is left in place for healing. A synthetic MUS should not be placed in the presence of a urethral injury [9].

Immediate Post-Operative Complications

Urinary Tract Infection

The AUA Guideline for the surgical management of SUI states that 4–15 % of women undergoing sling placement will report UTIs [9]. Urinary tract infections were the most common complication (11 % of patients) reported in the TOMUS trial for both RP and TOT slings [20]. A more recent study by

Gehrich et al. used the National Surgical Quality Improvement Program (NSQIP) to review data collected on 9851 patients who underwent a MUS. Of these, 3.4 % developed a post-operative UTI, which is consistent with rates published in previous literature [25].

Patients with typical symptoms of a UTI such as frequency, urgency, and/or hematuria should be evaluated with a urine culture. Those with severe, recurrent, or persistent symptoms may warrant a more thorough investigation including blood cultures, cross-sectional imaging, post-void residual, UDS, or cystoscopy when clinically appropriate. Abscesses, urinary obstruction, foreign bodies, sling perforation, or stones should all be included in the differential [21].

The current AUA best practice policy statement on urologic surgery antimicrobial prophylaxis recommends 24 h of therapy for vaginal surgery [26]. However, a recent RCT of 149 patients by Jackson et al. evaluated the benefit of adding a 3-day antibiotic course post-operatively for patients undergoing vaginal surgery for SUI. Patients were randomized to a 3-day post-operative placebo ($n=75$) or nitrofurantoin (100 mg 2 times a day) ($n=74$). Overall, 37 (24.8 %) women were diagnosed with a UTI within the 6-week post-operative study period. The incidence was significantly lower in the treatment arm (17.6 %) compared to placebo (32 %), ($p=0.04$) [27]. This may suggest a potential benefit to a short course of antibiotic prophylaxis but further studies are warranted.

Lower Urinary Tract Symptoms

Lower urinary tract symptoms or overactive bladder (OAB) can occur after placement of a MUS in patients without any previous OAB symptomatology. De novo urge incontinence or UUI is often transient and may resolve spontaneously. In such cases, patients should be counseled and reassured. However, a quarter of patients may have persistent symptoms that require intervention [28]. The rate of de novo urge incontinence has been estimated previously as 6 % [9]. A series of 463 patients reported de novo urgency in 14.5 % of patients undergoing a MUS. They identified significant risk factors of developing de novo urgency as older age and parity [29]. A study by Lee et al. also evaluated risk factors for developing de novo urgency or UUI. They identified 358 women with SUI or mixed urinary incontinence who underwent a MUS. De novo urgency occurred in 27.7 % of patients and de novo UUI occurred in 13.7 %. Intrinsic sphincteric deficiency, previous surgery for SUI or prolapse, colposuspension, and/or preexisting detrusor overactivity increased the risk of post-operative urgency or UUI [30].

Reversible causes of de novo urgency/UUI should be evaluated and treated accordingly. A recent review by Abraham and Vasavada cited that de novo urgency occurs in 6 % of patients and modifiable causes include post-operative UTI (7.4–14.7 %), bladder outlet obstruction (BOO) (1.9–

19.7 %), and perforation of the urinary tract (0.5–5 %), with 0–28 % of cases occurring due to idiopathic etiologies [31]. On the other hand, it has been also been proposed that a MUS can actually improve OAB symptoms. A study by Segal et al. retrospectively reviewed 98 MUS patients and found that approximately 57 % of patients with OAB demonstrated resolution of their symptoms, while only 4.3 % reported de novo OAB [32].

Treatment options for urgency or UUI post-MUS are similar to those for uncomplicated OAB and first include behavioral modification such as bladder training, bladder control strategies, pelvic floor muscle training, and/or fluid management. According to the updated AUA Guidelines for OAB, this may be combined with antimuscarinics or beta-3 agonists as options for second-line therapy, and sacral neuromodulation, onabotulinumtoxinA, or peripheral tibial nerve stimulation (PTNS) for refractory OAB [33]. Of note, a recent study by Serati et al. found that in the setting of de novo OAB after a MUS, solifenacin had significantly lower efficacy compared to controls [34]. OnabotulinumtoxinA, however, showed similar efficacy in a prospective study of 102 women comparing those with idiopathic OAB ($n=53$) to women with de novo OAB post-MUS ($n=49$) in a study by Miotla et al. [35].

Delayed Post-Operative Complications

Diagnostic Evaluation

The clinical evaluation should begin with a detailed clinical history and a high index of suspicion as mesh-related complications can be subtle and difficult to identify. Patients should be assessed for voiding dysfunction, dyspareunia, hispareunia (painful intercourse secondary to a mesh exposure that is reported by the male partner) [36], vaginal discharge or bleeding, pelvic/groin pain, urinary incontinence, hematuria, and recurrent UTIs. A complete surgical history, the clinical time course of symptom presentation, and information about previous treatments should also be obtained. Acquiring the previous operative records is also paramount to confirm what type of mesh and surgical approach were used. It is noteworthy, however, that those patients, who present without complaints of the aforementioned symptomatology and report no mesh-related complications, should not undergo a sling excision unless bothersome symptoms develop [11]. It can also be helpful to utilize standardized questionnaires to assess baseline symptomatology as well as monitor for improvement throughout subsequent therapies.

A physical exam, including a thorough abdominal and pelvic exam, should be performed. Attention should be directed at identifying vaginal discharge or bleeding, granulation

tissue, scar tissue contraction or banding, foreign body exposure or palpation, or reproducible areas of tenderness or discomfort. At times, an exam under anesthesia may be required to ensure a complete examination, especially if significant pain or difficult body habitus are present. A urinalysis should be obtained to assess for UTI and hematuria, with urine culture, if indicated. Measuring post-void residual urine volumes can identify urinary retention or incomplete emptying.

Cystourethroscopy should always be performed if there is any suspicion for a mesh-related complication. This can identify a mesh perforation within the bladder or urethra. Urodynamics (UDS) should also be performed for patients who present with voiding dysfunction. This can help to identify iatrogenic bladder outlet obstruction (BOO) or de novo or persistent detrusor overactivity. Videourodynamics (VUDS) may also be helpful as it can help to identify urethral narrowing or kinking and associated proximal urethral dilation at the level of the MUS during a sustained detrusor contraction [37, 38].

While imaging has not been used routinely in this setting, pelvic imaging with a CT scan or MRI may be warranted if there is concern for a pelvic abscess or infection. A bladder wall indentation or distortion of the urethral wall may also be apparent. Nevertheless, the use of pelvic CT or MRI for sling identification is a novelty, and the actual sling may be difficult to visualize. On the other hand, translabial ultrasonography has been utilized to aid in both preoperative and intraoperative identification of the sling. A study by Staack et al. compared the clinical versus definitive operative findings of 51 women who were undergoing surgical MUS excision. The study was able to accurately locate the position of the mesh sling and identify the type (RP vs. TOT) [39].

Management Options

Pain and Dyspareunia

Vaginal and/or pelvic pain, associated with or without dyspareunia, can be a quite difficult clinical presentation to evaluate and manage. Pain in the setting of a MUS can occur from a myriad of etiologies. These can include excessive tensioning of the MUS, scarring or local nerve irritation, a low-grade infection, or can be completely unrelated to the MUS itself [40]. This discomfort can be transient in nature and resolve spontaneously, or may require more invasive treatments.

Unfortunately, MUS excision may not be curative and debilitating pain can still result. A study by Danford et al. evaluated the post-operative pain of 233 patients who were undergoing a mesh excision for the indication of pelvic pain after a MUS. The study found that 73 % of patients reported improvement in their pain, with 18 % reporting worsening of their pain, and 19 % reporting the pelvic pain was unchanged post-operatively [41]. Hou et al. found similar results in

patients who presented with pelvic pain after a MUS. In their study of 54 patients who underwent vaginal mesh excision, 67 % reported being “pain-free” as indexed by a visual analog scale (VAS) score of zero [42].

While these studies show a benefit to performing a MUS excision for pain, the amount of mesh that is able to be safely excised is unpredictable, and various surgical techniques are available as treatment options. Our practice is to perform a vaginal mesh excision and employ an inverted U incision to access the retropubic space with the goal of excising the entire suburethral portion and the maximum allowable length of the mesh arms. A cystoscopy should also be performed during this time.

Groin pain is also a recognized complication of MUS, especially with the TOT approach. It has been reported in up to 4 % of patients after a TOT MUS [21]. While the pain can be temporary, it may also be intractable requiring mesh excision. In extreme cases of debilitating leg and groin pain, we have made an additional lateral groin incision over the inferior pubic ramus at the level of the obturator foramen. This is typically performed in conjunction with orthopedic surgery to completely remove the MUS arms and has produced positive outcomes in the majority of patients [43].

In addition to pain, dyspareunia is a frequently reported complication after both RP and TOT MUS surgery. Petri and Ashok reported late sling complications in 280 women. Of these patients, 3 % reported dyspareunia with a RP MUS, while 18 % reported persistent dyspareunia after a TOT sling [44]. Dyspareunia may be transient and conservative measures should be offered, but persistent dyspareunia can occur. In such cases, improved sexual function has been reported after sling excision. Kuhn et al. performed a sling excision in 18 patients who all reported improvement in sexual function post-operatively [45].

Male partners have also reported dyspareunia “hispareunia” in the presence of a mesh erosion in the female partner. A study by Mohr et al. evaluated sexual function in 32 males before and after their partners underwent a MUS excision for a mesh exposure. Using the VAS to assess pain with intercourse, the mean VAS score improved from 8 to 1 after intervention, suggesting that sexual interest and drive may be negatively influenced and can be treated effectively by correcting the MUS exposure in the female partner [36].

Nevertheless, a recent TOMUS trial follow-up study stated that MUS surgery can be beneficial for sexual function. The study reported a significant improvement in dyspareunia, incontinence during sex, and fear of incontinence during sex after a MUS procedure for both TOT and RP approaches. Self-reported data showed that 153 of the 406 (38 %) sexually active women reported dyspareunia preoperatively. After the MUS procedure, dyspareunia was reported by 7 % of women 12 months after surgery ($p=0.003$) [46].

Vaginal Mesh Exposure

Vaginal mesh exposure is one of the most common complications of MUS. Mesh exposure rates range from 0 to 8.1 % in the literature, though these numbers may be underreported due to the aforementioned changes in terminology and lack of reporting [47]. Asymptomatic exposures can be observed, and many will advocate for a trial of topical estrogen cream for a small exposure; however, there are few data that support this and the current literature reports mixed efficacy [48, 49]. Failure of the vagina to re-epithelialize warrants excision or vaginal closure. As such, many providers will recommend a vaginal mesh excision as the primary treatment. There is not currently a consensus on how much mesh should be removed or how far the dissection should be carried from the exposed area. For a minimally invasive approach, only the small portion of exposed mesh is excised [50]. However, performing a formal mesh excision with removal of the mesh arms has been our practice as previously described. Excision of vaginal mesh should not be minimized, as the procedure can be technically quite difficult and often requires multiple procedures.

Bladder Outlet Obstruction

Bladder outlet obstruction (BOO) can present in a variety of ways and, as a result, the true incidence is difficult to accurately assess. The rate of urinary retention (catheter dependency for at least 28 days) is estimated to occur after 1–10 % of MUS [9, 51]. However, patients may also complain of incomplete emptying, de novo frequency and urgency, UUI, hesitancy, straining to void, weak stream, recurrent UTIs, or dysuria. This can be evaluated with a pressure-flow (PF) study on UDS and a post-void residual. As in men with BOO, the PF tracing may show a high voiding pressure and low flow rate. However, there is no consistent index value for BOO in women and the absence of “high pressure, low flow” on UDS does not rule out iatrogenic obstruction [52, 53].

Treatment choice for BOO varies widely according to surgeon or patient preference as well as individual patient factors. Non-surgical therapies may be offered for minimal obstruction such as self-intermittent catheterization (SIC), indwelling catheterization, urethral dilation, medical management, or bio-feedback [22]. However, these therapies are limited and surgical intervention is often necessary including: sling loosening, sling incision, sling excision, or urethrolisis (infrapubic, retropubic, or transvaginal) [54].

Often times, there is residual edema after the procedure leading to urinary retention. Spontaneous voiding should occur within 1 week. If the patient cannot void spontaneously at that time, loosening the sling has been reported in the literature. Advocates of this technique recommend making a small vaginal incision and using a right angle clamp to gently loosen the MUS [55]. A sling incision can also be performed to

release the tension on the MUS complex [56]. While this can resolve the BOO, it can also lead to recurrent incontinence. A sling excision or urethrolisis is also an option for management of BOO, especially when the clinical presentation is delayed. As such, it is our practice to perform a mesh excision and safely remove the maximum amount of mesh possible, which includes entering the retropubic space to remove the mesh arms. We will also perform a concomitant urethrolisis as indicated. Cure rates for urethrolisis in the setting of a MUS are variable as much of the data is extrapolated from pubovaginal slings.

It has been postulated that delayed surgical intervention of BOO may not necessarily improve micturition, and longstanding obstruction of the urethra can have an irreversible impact. In fact, persistent voiding dysfunction after urethrolisis has been reported in the literature. In a series by Starkman et al., approximately 50 % of patients reported persistent overactive bladder (OAB) symptoms following urethrolisis. The study evaluated 40 patients with obstructive urinary symptoms, 36 of whom reported OAB symptomatology at presentation. After urethrolisis, 56 % reported refractory OAB and were continued on antimuscarinics post-operatively, with 8 ultimately undergoing sacral neuromodulation [57, 58]. As such, prompt diagnosis of BOO and early intervention is prudent.

Mesh Perforation and Urinary Fistula

Pelvic surgeons should always retain a high index of suspicion for LUT mesh perforation, as it can present with a wide range of symptoms and findings. The true incidence of mesh perforations is unknown, but it is estimated to be 0.7–5 % for retropubic slings and 0–0.5 % for transobturator slings [31, 59]. It is unclear whether a mesh perforation results from progressive erosion of the mesh over time or from a missed perforation at the time of the procedure [22]. Of note, the TOMUS trial did not identify any urethral or bladder perforations for transobturator slings [21]. Various etiologies leading to mesh exposure include sling tension, extensive vaginal dissection resulting in devascularization of the urethra, missed trocar injury at the time of MUS placement, traumatic catheterization or dilation, or compromised urethral vascularity such as from estrogen deficiency [22]. Patients with a mesh perforation can present with variable symptomatology. In a retrospective review by Osborn et al., 27 patients were identified to have a post-operative MUS perforation (bladder perforation $n=12$, urethral perforation $n=15$). Of these, 11/27 (41 %) presented with irritative voiding symptoms, 7/11 (26 %) incontinence, 4/11 (15 %) vaginal pain, and 2/11 (7 %) with either recurrent UTIs or dyspareunia [59].

Mesh perforation typically mandates surgical excision; however, this may be performed in a variety of approaches. For a small, isolated mesh segment within the urinary tract,

endoscopic management with either the holmium laser, scissors, or transurethral resection has been described [60, 61]. However, most mesh perforations require a transvaginal and/or abdominal exploration and excision, closure of the urinary tract, and post-operative urinary drainage. An interposition graft may also be required. Shah et al. described a series of 21 patients with mesh perforation after MUS who underwent a transvaginal or transvaginal/transabdominal mesh excision, urinary tract reconstruction, and concomitant pubovaginal sling with autologous rectus fascia. Of these, 100 % had complete resolution of their presenting symptoms. All of the patients with mesh perforations of the bladder were continent, and 10/14 (71.5 %) with urethral perforations were continent post-operatively [62].

Unrecognized or untreated mesh perforations can also lead to fistula formation; fistulae can also develop after an attempt to treat prior mesh complications. Blaivas and Mekel reported a series of 10 women who presented with urinary fistulas after MUS placement. Patients presented with SUI (70 %), unaware incontinence (50 %), OAB (40 %), pelvic pain (30 %), and voiding symptoms (20 %). Of these 7/10 underwent a successful fistula repair. One of the patients had a urinary diversion while the other 9/10 underwent primary repair with an interposition graft (Martius flap, omental flap, bladder wall flap, or autologous sling) [63]. While the majority of patients in this series had a successful repair, results can be quite variable.

Long-term Sequelae

Unfortunately, despite multiple attempts at surgical revision, complications from MUS can be quite morbid. Blaivas et al. reported a retrospective review of 47 women who had previously undergone at least 1 operation to correct MUS complications [64]. With a mean follow-up of 3 years, 72 % of patients had a successful outcome after the first procedure. Of the 13 patients with treatment failure, 9 patients underwent a total of 14 salvage operations. This purports that though treatment success is possible, multiple procedures may be required. Another study by Hansen et al. evaluated 111 patients with complaints of complications from vaginal mesh. Of these, 37 % had undergone a MUS (mean 2.4 years prior) and were presenting to the tertiary care facility for further intervention. Results from the administered, validated questionnaire showed patients commonly reported problems with their “emotional health” or “feeling frustrated” suggesting that these sequelae can significantly impact a patient’s quality of life [65]. As such, prior to any procedure for the management of a MUS complication, preoperative counseling should include a thorough discussion of realistic outcomes.

Conclusion

Complications from MUS are not rare. The MUS should be inserted according to the standard guidelines by an experienced surgeon to reduce the incidence of complications. However, if a patient does have post-operative concerns, providers should have a high index of suspicion for mesh-related complications. The management of MUS complications is challenging and may warrant referral for specialist care. Unfortunately, these complications are not always reversible and can be quite debilitating for patients. Nevertheless, despite the risk of complications, the MUS remains the standard of care for the surgical treatment of SUI for many practitioners.

Compliance with Ethical Standards

Conflict of Interest Drs. Brown, Cohn, and Reynolds declare no conflict of interest.

Dr. Kaufman declares the following relationships: Cook Myosite (global principal investigator) and American Medical Systems (resident teaching course faculty).

Dr. Dmochowski declares the following relationships: Allergan (consultant), Medtronic (consultant).

Human and Animal Rights and Informed Consent This article does not contain studies with human or animal subjects performed by the author.

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